

FIG. 1

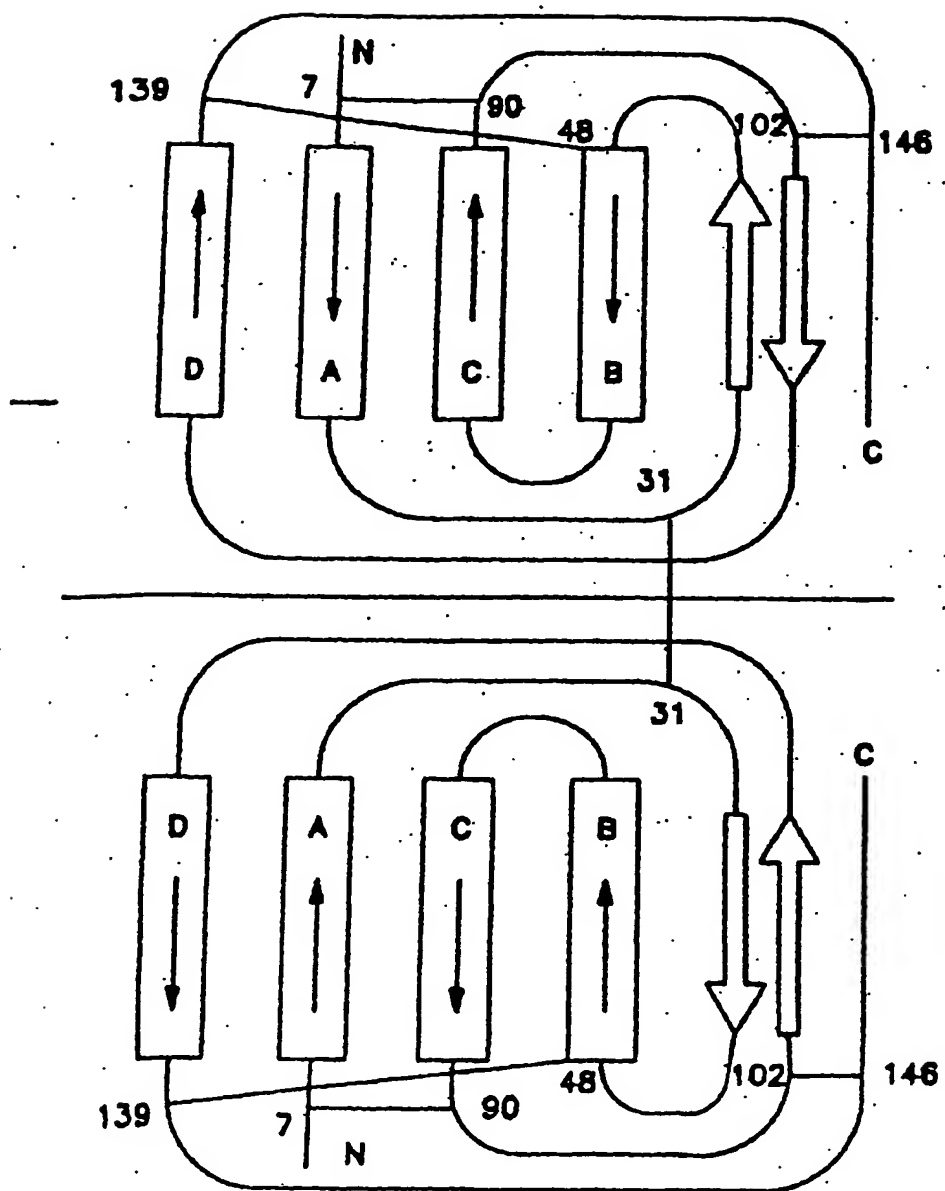


FIG. 2

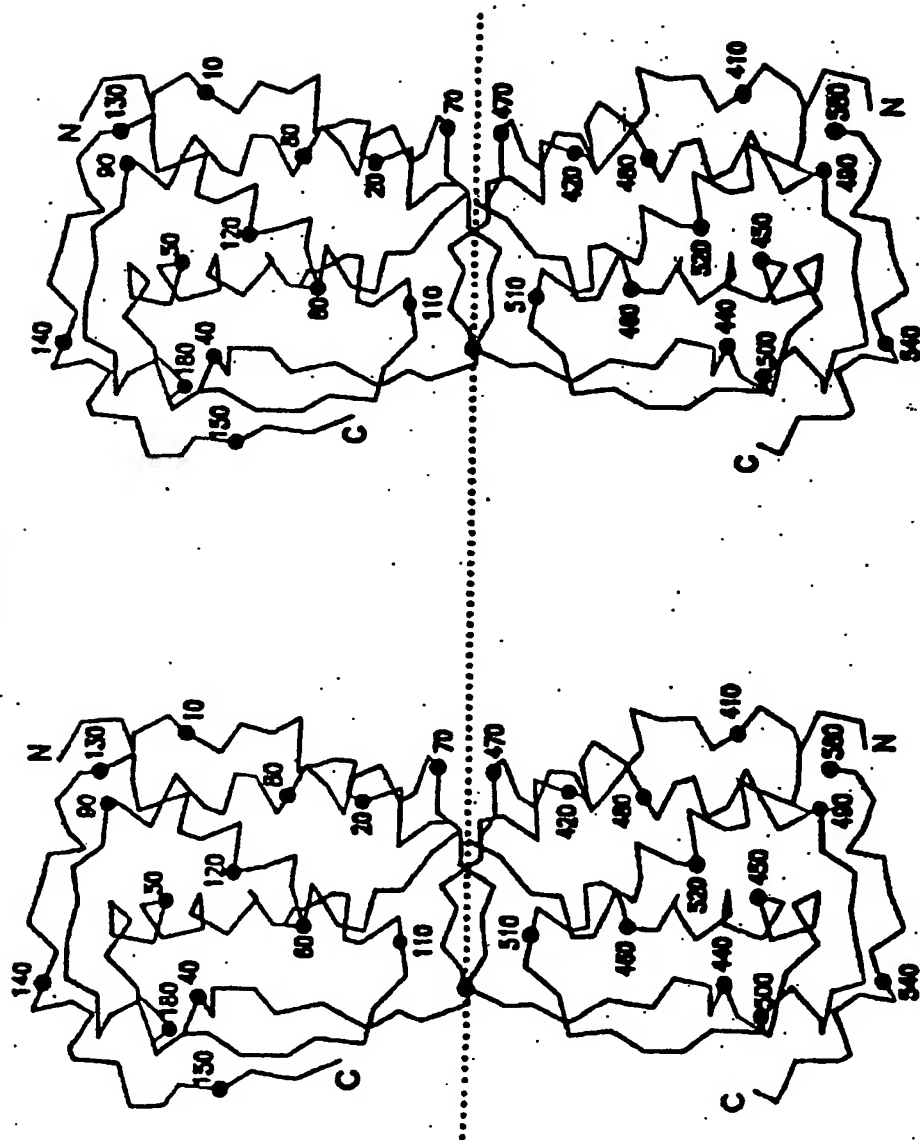


FIG. 3

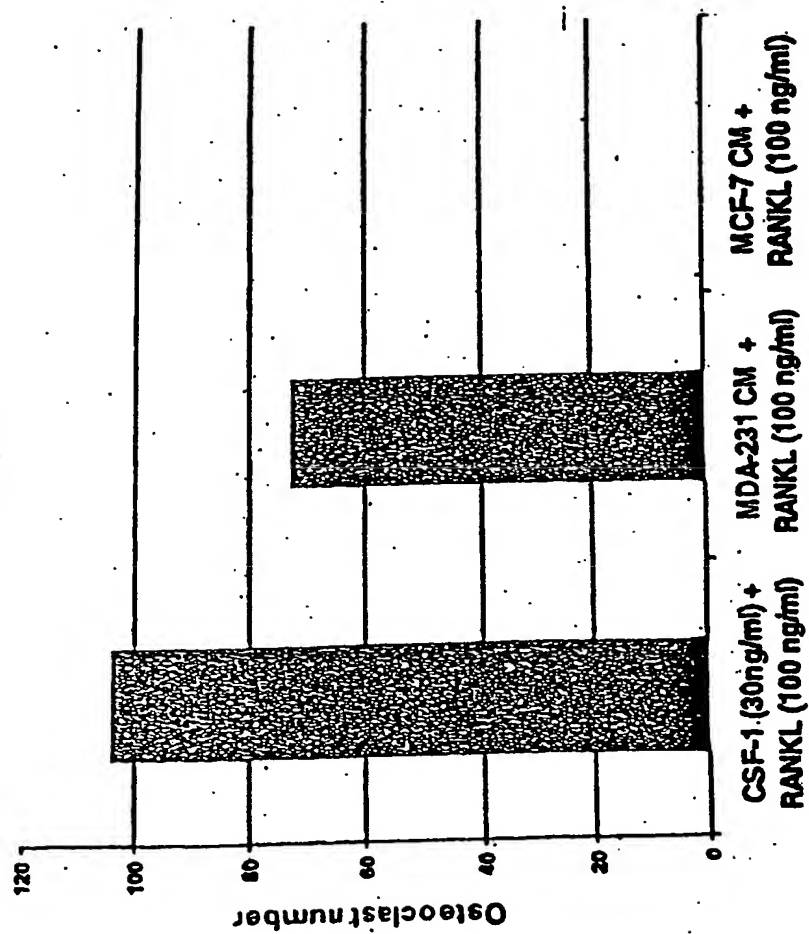


FIG. 4B

CHIR-R1X Light Chain Risk Assignments

V-Region	Amino Acids 1-52
Risk	LHLHLMLMLHLMLLLHLHLHLMHHHHHHHHHHHMLMLMHMHHHHHH
Mouse	DILLTQSPAILSVSPGERVSFSCRASQSIGTSIH----WYQQR ^T NGSPRL ^L LTKYAS

V-Region	Amino Acids 53-109
Risk	HLMMHLHMLHLHLHLHLHLHLHLHLHLHHHHHHHHHHHHHHHHHLHLHLHLHL
Mouse	ESISGIP ^S RFSGSGGTDF ^T LSINSVESEDIADY ^C QQINSWPT-----TFGGGT ^K LEI-KRA

FIG. 4C

CHIR-RX1Heavy Chain Risk Assignments

V-Region	Amino Acids 1-57
Risk	MHLHLHLMLMLMLLLHLHLHLMMHHHHHHHHHHHMLMLLMHMMHHHHHHHHHHHH
Mouse	DVQLQESG <u>P</u> GLV <u>K</u> PSLSLTCTVT <u>D</u> YSITSDYAWN-WIRQ <u>F</u> PGNK <u>L</u> EW <u>M</u> G <u>Y</u> IS---YSGST
V-Region	Amino Acids 58-113
Risk	HMHHMMHMLMHLHLHLMLMLHLHLHLHLHLHLMMHHHHHHHHHHHHHHHHHHHHHLHLHLHL
Mouse	SYNP <u>S</u> L <u>K</u> S <u>R</u> I <u>S</u> ITRD <u>T</u> SKNQFFLQ <u>L</u> NSVT <u>T</u> EDTATYYCASFDYA <u>H</u> AM-----DYWGQGT <u>S</u> VT <u>V</u> SS

FIG. 5A

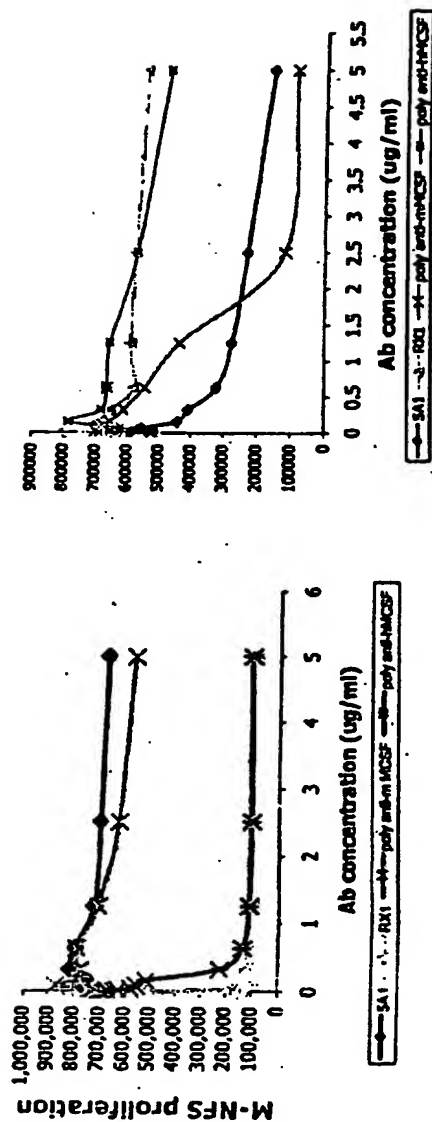
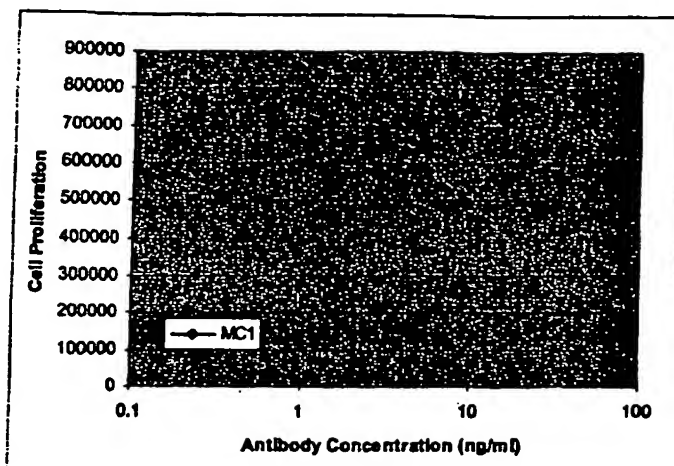


FIG. 5B

MC1 Neutralizes human MCSF activity



MC3 Neutralizes human MCSF activity

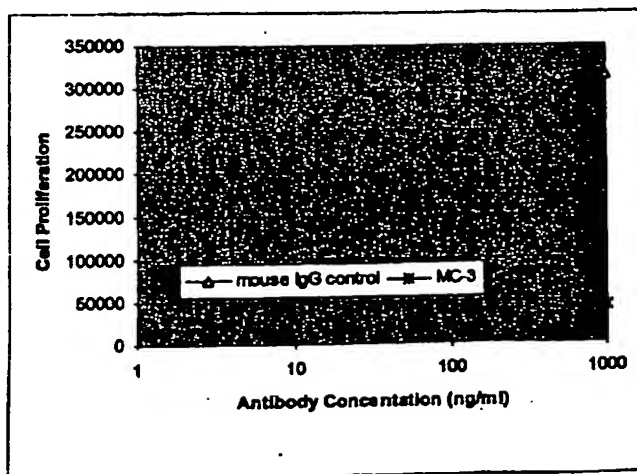


Fig. 6

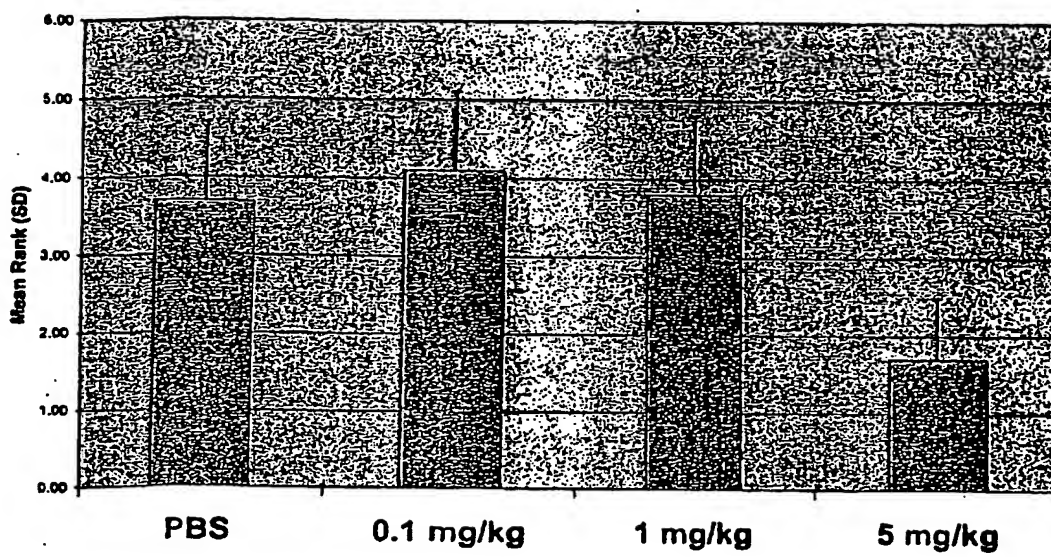


Fig. 7

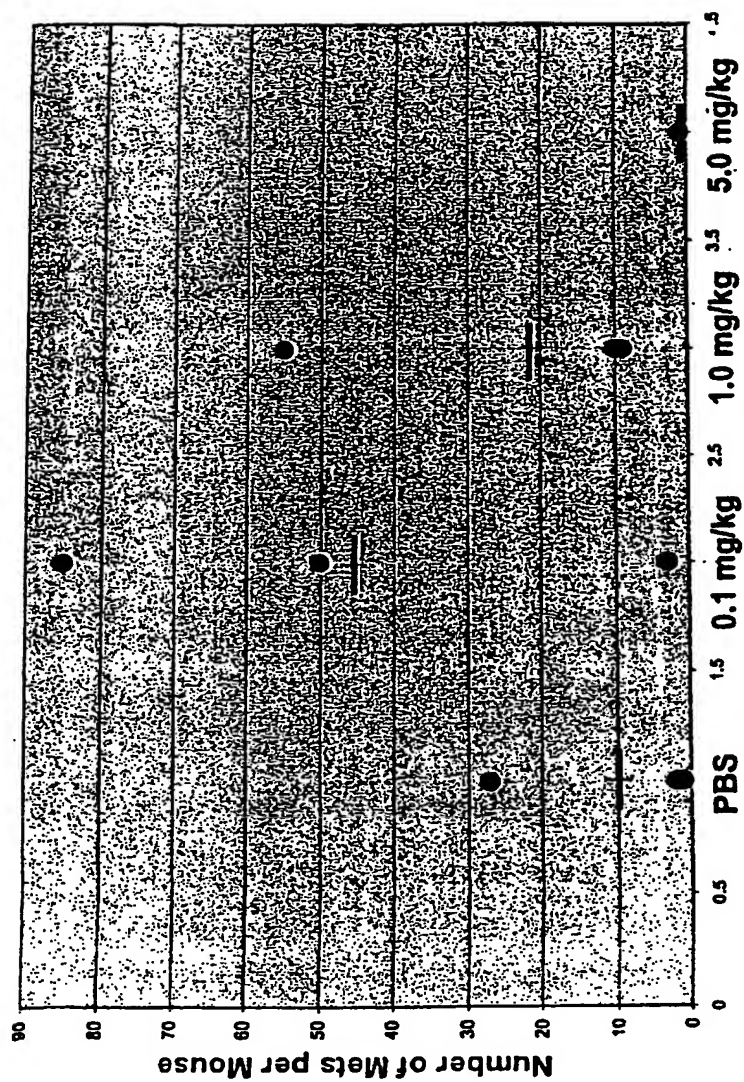
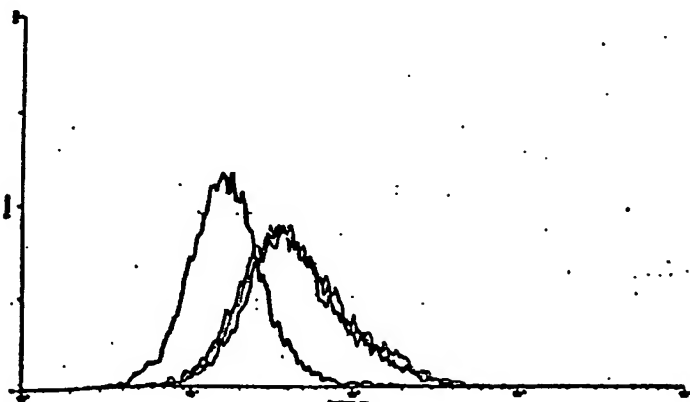


FIG. 8A

Binding of MCSF-specific antibody to breast cancer cell line MDA231

Red: no antibody control
Black: M-CSF antibody 1 ug/ml
Green: M-CSF antibody 10 ug/ml
Blue: M-CSF antibody 50 ug/ml

**FIG. 8B**

Binding of MCSF-specific antibody to multiple myeloma cancer cell line ARH77

Red: no antibody control
Green: M-CSF antibody 5 ug/ml
Blue: control IgG2a 5 ug/ml

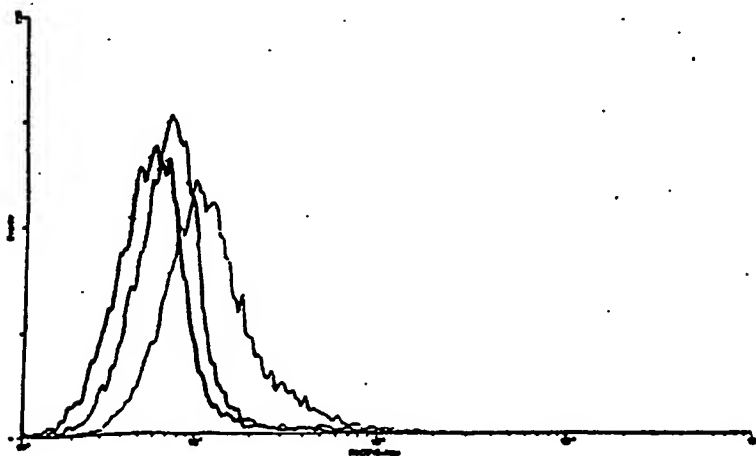


FIG. 9

Cancer Type	Cancer Status	Score 0	Score 1	Score 2	Score 3	Score 4	% with scores 3 or higher
adrenal	normal	10	5	5	0	0	0
basal cell	cancer	5	0	0	0	0	0
bladder	normal	6	1	2	1	0	10
brain	normal	17	1	2	0	0	0
breast	cancer	6	5	13	62	0	72
breast	normal	7	5	7	6	0	24
carcinoids	cancer	9	2	2	0	0	0
carcinoids (muscle)	cancer	1	0	1	0	0	0
choriocarcinoma	cancer	1	0	0	0	0	0
colon	normal	4	0	2	0	0	0
colon	cancer	9	0	1	4	0	27
fibrosarcoma	cancer	3	1	0	0	0	0
gallbladder	normal	2	1	0	1	0	26
germ cell	cancer	1	0	0	0	0	0
heart	normal	7	3	2	4	0	26
kidney	normal	5	10	1	4	0	20
kidney	cancer	8	1	0	3	0	25
leiomyosarcoma	cancer	5	0	0	0	0	0
liver	normal	11	3	4	1	0	8
liver	cancer	5	3	0	3	0	27
lung	normal	19	0	1	0	0	0
lung	cancer	3	1	0	3	0	43
lymphoma	cancer	13	0	3	2	0	12
melanoma	cancer	7	0	2	5	0	36
melanoma (inflammation)	cancer	0	0	0	1	0	100
mesothelioma	cancer	6	0	0	0	0	0
neuroblastoma	cancer	1	0	0	0	0	0
ovary	normal	6	0	2	0	0	0
ovary	cancer	8	2	0	4	0	29
pancreas	normal	9	2	5	4	0	20
pancreas	cancer	8	1	0	3	0	26
prostate	normal	0	3	8	3	0	21
prostate	cancer	9	1	1	4	0	27
sarcoma all	cancer	6	0	2	2	0	20
sarcoma	cancer	3	0	2	1	0	17
sarcoma (kidney)	cancer	3	0	2	1	0	17
sarcoma mth	cancer	2	0	0	0	0	0
seminoma	cancer	3	0	0	0	0	0
small intestine	normal	2	1	0	1	0	25
spleen	normal	14	2	3	0	0	0
squamous cell	cancer	3	0	0	0	0	0
stomach	normal	3	2	2	1	0	13
stomach	cancer	7	1	1	1	0	10
teratoma	cancer	1	0	0	0	0	0
testis	normal	5	1	3	3	0	25
thyroid	normal	15	0	0	0	0	0
thyroid	cancer	6	2	1	2	0	18
undiff all	cancer	6	0	2	1	0	11
undiff	cancer	5	0	2	0	0	0

Fig. 10

Met	Thr	Ala	Pro	Gly	Ala	Ala	Gly	Arg	Cys	Pro	Pro	Thr	Thr	Trp	Leu	1	5	10	15
Gly	Ser	Leu	Leu	Leu	Leu	Val	Cys	Leu	Leu	Ala	Ser	Arg	Ser	Ile	Thr	20	25	30	
Glu	Glu	Val	Ser	Glu	Tyr	Cys	Ser	His	Met	Ile	Gly	Ser	Gly	His	Leu	35	40	45	
Gln	Ser	Leu	Gln	Arg	Leu	Ile	Asp	Ser	Gln	Met	Glu	Thr	Ser	Cys	Gln	50	55	60	
Ile	Thr	Phe	Glu	Phe	Val	Asp	Gln	Glu	Gln	Leu	Lys	Asp	Pro	Val	Cys	65	70	75	80
Tyr	Leu	Lys	Lys	Ala	Phe	Leu	Leu	Val	Gln	Asp	Ile	Met	Glu	Asp	Thr	85	90	95	
Met	Arg	Phe	Arg	Asp	Asn	Thr	Pro	Asn	Ala	Ile	Ala	Ile	Val	Gln	Leu	100	105	110	
Gln	Glu	Leu	Ser	Leu	Arg	Leu	Lys	Ser	Cys	Phe	Thr	Lys	Asp	Tyr	Glu	115	120	125	
Glu	His	Asp	Lys	Ala	Cys	Val	Arg	Thr	Phe	Tyr	Glu	Thr	Pro	Leu	Gln	130	135	140	
Leu	Leu	Glu	Lys	Val	Lys	Asn	Val	Phe	Asn	Glu	Thr	Lys	Asn	Leu	Leu	145	150	155	160
Asp	Lys	Asp	Trp	Asn	Ile	Phe	Ser	Lys	Asn	Cys	Asn	Asn	Ser	Phe	Ala	165	170	175	
Glu	Cys	Ser	Ser	Gln	Gly	His	Glu	Arg	Gln	Ser	Glu	Gly	Ser	Ser	Ser	180	185	190	
Pro	Gln	Leu	Gln	Glu	Ser	Val	Phe	His	Leu	Leu	Val	Pro	Ser	Val	Ile	195	200	205	
Leu	Val	Leu	Leu	Ala	Val	Gly	Gly	Leu	Leu	Phe	Tyr	Arg	Trp	Arg	Arg	210	215	220	
Arg	Ser	His	Gln	Glu	Pro	Gln	Arg	Ala	Asp	Ser	Pro	Leu	Glu	Gln	Pro	225	230	235	240
Glu	Gly	Ser	Pro	Leu	Thr	Gln	Asp	Asp	Arg	Gln	Val	Glu	Leu	Pro	Val	245	250	255	

Fig. 11

Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu
 1 5 10 15
 Gly Ser Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr
 20 25 30
 Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
 35 40 45
 Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
 50 55 60
 Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
 65 70 75 80
 Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
 85 90 95
 Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
 100 105 110
 Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
 115 120 125
 Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
 130 135 140
 Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
 145 150 155 160
 Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
 165 170 175
 Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu
 180 185 190
 Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His
 195 200 205
 Gln Pro Leu Ala Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu
 210 215 220
 Asp Ser Glu Gly Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro
 225 230 235 240
 Leu His Thr Val Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser
 245 250 255
 Thr Cys Gln Ser Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser
 260 265 270
 Thr Ile Gly Gly Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn
 275 280 285
 Pro Gly Met Glu Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val
 290 295 300
 Pro Glu Glu Ala Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly
 305 310 315 320
 Thr Glu Leu Ser Pro Ser Arg Pro Gly Gly Gly Ser Met Gln Thr Glu
 325 330 335
 Pro Ala Arg Pro Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala
 340 345 350
 Ser Ala Lys Gly Gln Gln Pro Ala Asp Val Thr Gly Thr Ala Leu Pro
 355 360 365
 Arg Val Gly Pro Val Arg Pro Thr Gly Gln Asp Trp Asn His Thr Pro
 370 375 380
 Gln Lys Thr Asp His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro
 385 390 395 400
 Gly Ser Pro Arg Ile Ser Ser Leu Arg Pro Gln Gly Leu Ser Asn Pro
 405 410 415
 Ser Thr Leu Ser Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly
 420 425 430
 Ser Val Leu Pro Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp
 435 440 445
 Arg Arg Ser Pro Ala Glu Pro Glu Gly Gly Pro Ala Ser Glu Gly Ala
 450 455 460
 Ala Arg Pro Leu Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly
 465 470 475 480
 His Glu Arg Gln Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser
 485 490 495
 Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val
 500 505 510
 Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro
 515 520 525
 Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr
 530 535 540
 Gln Asp Asp Arg Gln Val Glu Leu Pro Val

Fig. 12

Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu
 1 5 10 15
 Gly Ser Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr
 20 25 30
 Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
 35 40 45
 Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
 50 55 60
 Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
 65 70 75 80
 Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
 85 90 95
 Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
 100 105 110
 Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
 115 120 125
 Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
 130 135 140
 Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
 145 150 155 160
 Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
 165 170 175
 Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu
 180 185 190
 Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His
 195 200 205
 Gln Pro Leu Ala Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu
 210 215 220
 Asp Ser Glu Gly Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro
 225 230 235 240
 Leu His Thr Val Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser
 245 250 255
 Thr Cys Gln Ser Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser
 260 265 270
 Thr Ile Gly Gly Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn
 275 280 285
 Pro Gly Met Glu Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val
 290 295 300
 Pro Glu Glu Ala Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly
 305 310 315 320
 Thr Glu Leu Ser Pro Ser Arg Pro Gly Gly Gly Ser Met Gln Thr Glu
 325 330 335
 Pro Ala Arg Pro Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala
 340 345 350
 Ser Ala Lys Gly Gln Gln Pro Ala Asp Val Thr Gly His Glu Arg Gln
 355 360 365
 Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser Val Phe His Leu
 370 375 380
 Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val Gly Gly Leu Leu
 385 390 395 400
 Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro Gln Arg Ala Asp
 405 410 415
 Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr Gln Asp Asp Arg
 420 425 430
 Gln Val Glu Leu Pro Val

FIG. 13**5H4 heavy chain protein sequence:**

```
1  EIQLQQSGPE LVKTGTSVKI SCKASGYSFT GYFMHWVKQS HGKSLEWIGY
51  ISCYNGDTNY NQNFKGKATF TVDTSSSTAY MQFNLSLTSED SAVYYCAREG
101 GNYPAYWGQG TLVTVSAAKT TPPSVYPLAP GSAAQTNSMV TLGCLVKGYP
151 PEPVTVTWNS GSLSSGVHTF PAVLQSDLYT LSSSVTVPSS TWPSETVTCN
201 VAHPASSTKV DKKIVPRDCG CKPCICTVPE VSSVFIFPPK PKDVLTTITLT
251 PKVTCVVVDI SKDDPEVQFS WFDVDDVEVHT AQTQPREEQF NSTFRSVSEL
301 PIMHQDWLNG KEFKCRVNSA AFPAPIEKTI SKTKGRPKAP QVYTIPPPKE
351 QMAKDKVSLT CMITDFFPED ITVEWQWNGQ PAENYKNTQP IMDTDGSYFV
401 YSKLNVQKSN WEAGNTFTCS VLHEGLHNNH TEKSLSHSPG K
```

5H4 light chain protein sequence:

```
1  DIVMTQSHKF MSTSVGDRVT ITCKASQNVG TAVTWYQQKP GQSPKLLIYW
51  TSTRHAGVPD RFTGSGSGTD FTLTISDVQS EDLADYFCQQ YSSYPLTFGA
101 GTKLELKRAD AAPTVISIFPP SSEQLTSGGA SVVCFLNNFY PKDINVWKWI
151 DGSERQNGVL NSWTDQDSKD STYSMSSTLT LTKDEYERHN SYTCEATHKT
201 STSPIVKSFN RNEC
```


FIG. 14**MC-1 heavy chain protein sequence:**

```
1   EVKLVESGGG LVQPGGSLKL SCATSGFTFS DYMYWVRQT PEKRLEWVAY
51  ISNGGGSTYY PDTVKGRTI SRDNAKNTLY LQMSRLKSED TAMYCARQG
101 SYGYPFAYWG QGTLVTVSAA KTTAPSVYPL APVCGDTTGS SVTLGCLVKG
151 YFPEPVTLTW NSGSLSSGVH TFPVQLQSDL YTLSSSVTVT SSTWPSQSIT
201 CNVAHPASST KVDKKIEPRG PTIKPCPPCK CPAPNLLGGP SVFIFPPKIK
251 DVLMLISLPI VTCVVVDVSE DDPDVQISWF VNNVEVHTAQ TQTHREDYNS
301 TLRVVSALPI QHQDWMSGKE FKCKVNNKDL PAPIERTISK PKGSVRAPQV
351 YVLPPPEEEM TKKQVTLTCM VTDFMPEDIY VEWTNNGKTE LNYKNTEPVL
401 DSDGSYFMYS KLRVEKKNWV ERNSYSCSVV HEGLHNHHTT KSFSRTPGK
```

MC-1 light chain protein sequence:

```
1   AIQMTQTSS LSASLGDRVT ISCSASQGIS NYLNWYQQKP DGTVKLLIYY
51  TSSLHSGVPS RFGSGSGSTD YSLTISNLEP EDIATYYCQQ YSKLPWTFGG
101 GTKLEIKRAD AAPTVSIFPP SSEQLTSGGA SVVCFLNNFY PKDINVKWKI
151 DGSERQNGVL NSWTDQDSKD STYSMSSTLT LTKDEYERHN SYTCEATHKT
201 STSPIVKSFN RNEC
```

FIG. 15**MC-3 heavy chain protein sequence:**

```
1   DVQLQESGPG LVKPSQSLSL TCTVTGYSIT SDYAWNWIRO FPGNKLEWMG
51  YISYSGSTSY NPSLKSRI SI TRDTSKNQFF LQLNSVTTED TATYYCARLE
101 TWLFDYWGQG TTLTVSSAKT TPSPVYPLAP GCGDTTGSSV TLGCLVKGYF
151 PESVTVTWNS GSLSSSVHTF PALLQSGLYT MSSSVTVPSS TWPSQTVTCS
201 VAHPASSTTV DKKLEPSGPI STINPCPPCK ECHKCPAPNL EGGPSVFIPP
251 PNIKDVLMI S LTPKVTCVVV DVSEDDPDVQ ISWFMNNVEV HTAQQTTHRE
301 DYNSTIRVVS TLPIQHQQDW SGKEFKCKVN NKDLPSPIER TISKIKGLVR
351 APQVYILPPP AEQLSRKDVS LTCLVVGFPN GDISVEWTSN GHTEENYKDT
401 APVLDSGDSY FIYKLN MKT SKWEKTD SFS CNVRHEGLKN YYLKKTISRS
451 PGLDLDDICA EAKDGELDGL WTTITIFISL FLLSVCYSAS VTLFKVKWIF
501 SSVVELKQKI SPDYRNMIQ GA
```

MC-3 light chain protein sequence:

```
1   DILLTQSPAI LSVSPGERVS FSCRASQSIG TSIHWYQORT NGSPRLLIKY
51  ASESISGIPS RFGSGSGGTD FTLSINSVES EDIADYYCQQ SNSWPTTFGG
101 GTKLEIKWAD AAPTVSIFPP SSEQLTSGGA SVVCFLNNFY PKDINVKWKI
151 DGSERQNGVL NSWTDQDSKD STYSMSSTLT LTKDEYERHN SYTCEATHKT
201 STSPIVKSFN RNEC
```

FIG. 16A

For heavy chain CDR1:

		1
H_CDR1_5H4	(1)	-G Y FMH
H_CDR1_MC-1	(1)	- Y YMY
H_CDR1_CHIR-RX1	(1)	SDY AWN
H_CDR1_MC-3	(1)	SDY AWN
Consensus	(1)	SDYAWN

For heavy chain CDR2:

		1	17
H_CDR2_5H4	(1)	YIS C NGD T NY N QNF K G	
H_CDR2_MC-1	(1)	YISNGGG S TY P D Y KG	
H_CDR2_CHIR-RX1	(1)	YIS- Y S G S T S Y N P S L K S	
H_CDR2_MC-3	(1)	YIS- Y S G S T S Y N P S L K S	
Consensus	(1)	YIS YSGSTSYNPSLKS	

For heavy chain CDR3:

		1
H_CDR3_5H4	(1)	-- G N YPAY
H_CDR3_MC-1	(1)	QGS K C PLAY
H_CDR3_CHIR-RX1	(1)	-F M L -HAM Y
H_CDR3_MC-3	(1)	--LET L E T
Consensus	(1)	DYGW FDY

FIG. 16B

For light chain CDR1:

	1	11
L_CDR1_5H4	(1)	ASONRE T
L_CDR1_MC-1	(1)	SASOGSNY N
L_CDR1_CHIR-RX1	(1)	ASO
L_CDR1_MC-3	(1)	ASO
Consensus	(1)	RASQSIGTSIH

For light chain CDR2:

	1
L_CDR2_5H4	(1) STRH
L_CDR2_MC-1	(1) SSLH
L_CDR2_CHIR-RX1	(1) ASIS
L_CDR2_MC-3	(1) ASIS
Consensus	(1) YTSEIS

For light chain CDR3:

	1
L_CDR3_5H4	(1) QO S ELT
L_CDR3_MC-1	(1) QO KLPWT
L_CDR3_CHIR-RX1	(1) QOIN P
L_CDR3_MC-3	(1) QQSN P
Consensus	(1) QQYSSWPTT

FIG. 17
Neutralization Activities of Intact mAbs vs. Fabs

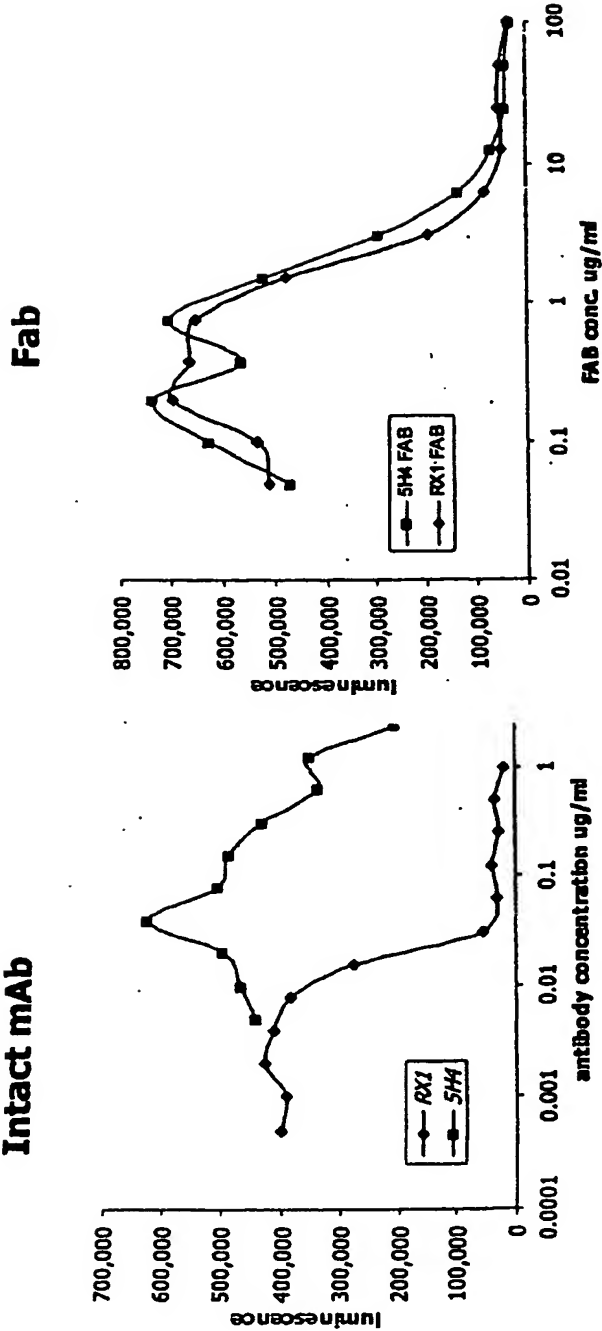


FIG. 18

MCSF Structure with RX1 Epitopes Highlighted

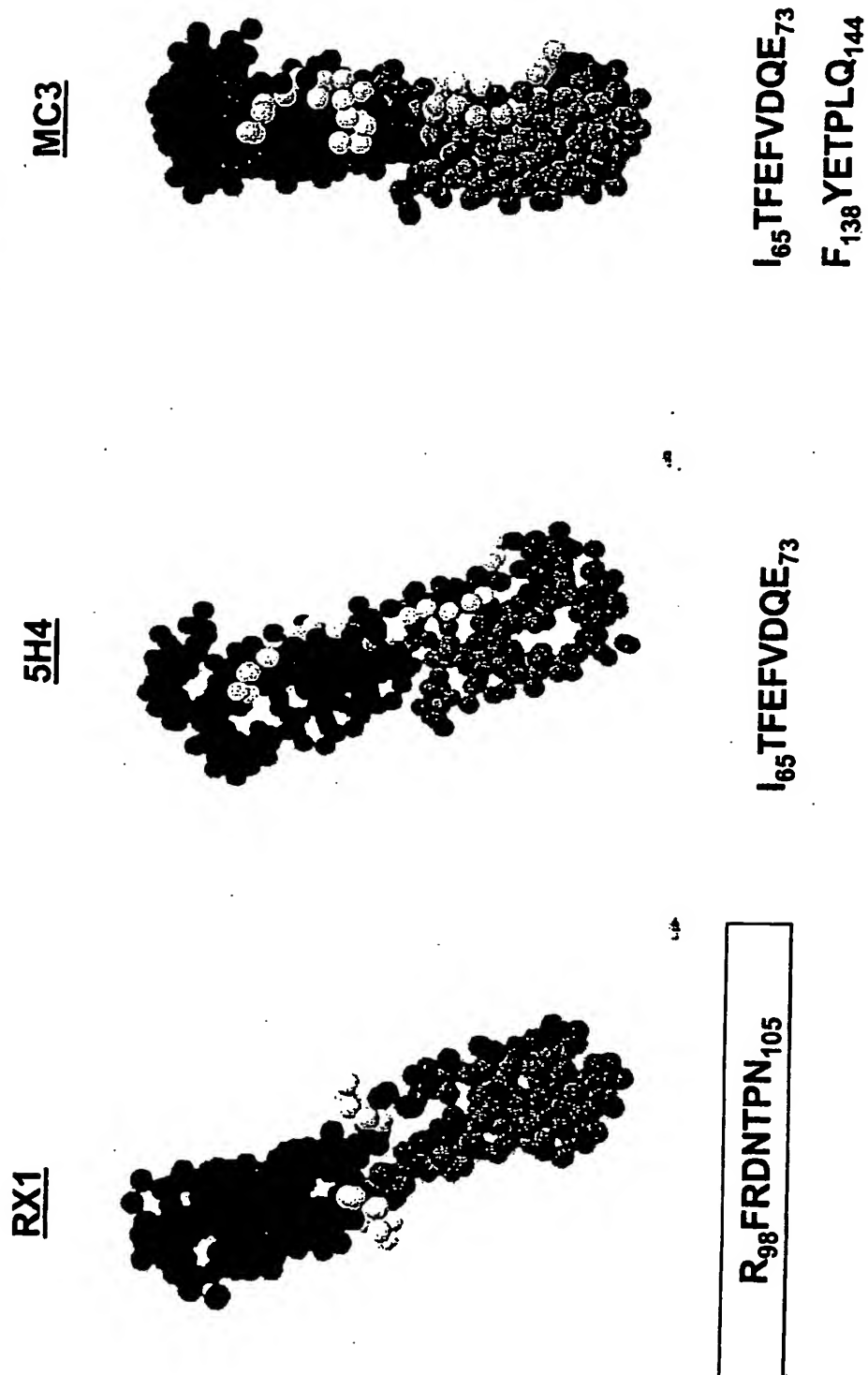


FIG. 19B**Low Risk Heavy Chain Vs. Kabat Vh2 Consensus:****Protein Seq:**

DVQLQESGPGLVKPSQTLSTCTVTVDYSITSDYAWNWRQFPGKKLEWMGYISYSGSTSYNPSLKSRTISRDTSKNQFSLQLNSVTAADTAVYYCASFDYAHAMD
YWGQGTTVTVSS

DNA Seq:

GACGTACAACCTCAAGAATCTGGCCAGGTCTCGTCAAAACCTTCTCAAACCTCTCACTCACTGCACTGTTACTGACTACTCTATTACATCCGACTACGCTT
GGAACCTGGATCCGACAAATTTCCTGGTAAATAAAGTGAATGGATGGGTTATATTCTTACTCTGGCTCCACCTCTCAAAATCCTTCTGAAATCACGCATCAC
AATTCCCGCGATACCTCTAAATAATCAATTTTCACTCCAACCTCAATTCTGTACCGCCCGGATAGTCCACCTACTACTGTGCCTCTTTTGACTACGCTCAOG
CCATGGATTATTGGGGACAGGGTACTACCGTTACCGTAAGCTCA

Low Risk + Moderate Risk Heavy Chain Vs. Kabat Vh2 Consensus:**Protein Seq:**

QVQLQESGPGLVKPSQTLSTCTVSDYSITSDYAWNWRQFPGKLEWMGYISYSGSTSYNPSLKSRTISRDTSKNQFSLQLNSVTAADTAVYYCASFDYAHAMD
YWGQGTTVTVSS

DNA Seq:

CAAGTTCAACTTCAAGAATCAGGCCCCGGACTCGTTAAACCTCTCAAACCTCTCTTACTTGCACTGTATCCGATTACTCTATTACTTCAGACTACGCTTG
GAACTGGATCAGACAAATTTCCCGGAAAGGACTCGAATGGATGGGATATATCTCTTACTCTGGCTCAACCTCTTACAAACCCCTCTCTCAAATCTCGAATAAC
AATCTCACGCGATCTTCTAAATAATCAATTCTCACTTCAACTAACTCCGTTACTGCCGCCGACACTGCCGTTTACTACTGTGCTTCTTCCGATTACGCCACG
CTATGGATTATTGGGGACAAGGAACCTACCGTCACTGTCAGCTCA

FIG. 20A

Light Chain

V-Region	No. of Changes	Amino Acids 1-52
Risk		LHLHLMLMLMLMLLLHLHLHLMLMHHHHHHHHHHHMLMLLMHHHHHHHH
Mouse		DILLTQSPAILSVSPGERVSFSCRASQSIGTSIH---WYQRTNGSPRLLIKYAS
Human		EIVLTQSPGTLSPGERATLSCRASQSVSSYL---AWYQQKPGQAPRLLIYGAS
Low Risk	8	EIVLTQSPGTLSPGERVTFSKRASQSIGTSIH---WYQKTKGQSPRLLIKYAS
Low+Mod	9	EIVLTQSPGTLSPGERVTFSKRASQSIGTSIH---WYQKTKGQAPRLLIKYAS

V-Region	No. of Changes	Amino Acids 53-109
Risk		HLMLHMLMHL
Mouse		ESISGIPSRFSGSGSGTDFTLTINSVESEDIADYVCQQINSWPT-----TFGGGTKLEI-KRA
Human		SRATGIPDRFSGSGSGTDFTLTISRLeDFAVYVCQYgsspp-----xTFGqGTKvEI-KRT
Low Risk	8	ERISGIPDRFSGSGSGTDFTLTISRVESEDFADYVCQQINSWPT-----TFGGGTKLEI-KRT
Low+Mod	10	ERATGIPDRFSGSGSGTDFTLTISRVESEDFADYVCQQINSWPT-----TFGGGTKLEI-KRT

FIG. 20B

Low Risk Light Chain Vs. Kabat Vk3 Consensus:**Protein Seq:**

EIVLTQSPGTLSPGERVTFSCRASQSIGTSHWYQQKTGQSPRLLIKYASERISIPDRFSGSGSDFTLTISRVESEDFADYYCQQINSWPTTFGQGTKLEIKRT

Nucleotide Seq:

GAAATAGTCCTTACCCAAATCTCCCGGAACCCCTCTCAGTATCTCCCGGGAACGAGTAACCTTTTCATGTAGAGCATCCCAATCCATCGGCACCTTCAATTCACT
GGTATCAGCAGAAACAGGTCAAATCCCCACGGCTTCTTATAAAATATGCATCAGAAAGAAATATCAGGCATTCCAGACAGATTTCTCAGGTTTCAGGTCAGGC
ACAGACTTCACACTTACAAATTTCCCGGTCGAATCCGAAGACTTCGCTGACTATTACTGCCAACAAATCAACTCATGGCTACTACTTTCGGTCAAGGCAACC
AAACTCGAAATTAAACGTACG

Low Risk + Moderate Risk Light Chain Vs. Kabat Vk3 Consensus:**Protein Seq:**

EIVLTQSPGTLSPGERVTFSCRASQSIGTSHWYQQKTGQAPRLLIKYASERATGIPDRFSGSGSDFTLTISRVESEDFADYYCQQINSWPTTFGQGTKLEIKRT

Nucleotide Seq:

GAAATAGTCTTACTCAAATCCCGCGGTACACTCTCAGTTTCCCAGGCAACGCGTCACCTTTTCTGCAGAGCATCACAATCAATCGGCACCTTCAATTCAATT
GGTATCAACAAACAGGACAGGCCCCACGACTTCTTATAAAATATGCATCAGAACGACGATCCAGATCCAGATTTTCAGGTTTCAGGATCAGGC
ACCGATTTCACACTTACAAATATCCAGAGTCGAATCAGAAAGATTTTCAGATTACTATTGTCAACAAATAAACGCTGGCCCCACTACATTCGGACAAAGGCACA
AAACTCGAAATTAAACGTACG

FIG. 21A

Light Chain – Changes back to Murine

V-Region	No. of Changes	Amino Acids 1-52
Risk		LHLHLMLMLHLMLLHLHLHLHLMLMHHHHHHHHHHMLLMHHHHHHHHH
Mouse		DILLTQSPAILSVSPGERVSFSCRASQSIGTSTIH---WYQQRTNGSPRLLIKYAS
Human		EIVLTQSPgTSLSPGERaTLCRASQSVssyL---AWYQQkPGQAPRLLIYGAS
Low Risk	8	EIVLTQSPGTLSPGERVTFCRASQSIGTSTIH---WYQQKTGQSPRLLIKYAS
Low+Mod	9	EIVLTQSPGTLSPGERVTFCRASQSIGTSTIH---WYQQKTGQAPRLLIKYAS

V-Region	No. of Changes	Amino Acids 53-109
Risk		HLMLHLMLHLHLHLHLHLHLHLHLHLHLHLHLHLHLHLHLHLHLHL
Mouse		ESISGIPSRFSGSGGTDFTLINSVESEDIADYYCQINSWPT-----TFGGGTKLEI-KRA
Human		sRATGIPdRFSGSGGTDFTLTIsrLepEDFAVYVCQYgsapp-----xTFGgGTKVei-KRT
Low Risk	8	ERISGIPDRFSGSGGTDFTLTISRVESEDFADYVCQINSWPT-----TFGQGTKLEI-KRT
Low+Mod	10	ERATGIPDRFSGSGGTDFTLTISRVESEDFADYVCQINSWPT-----TFGQGTKLEI-KRT
Low+Mod Alternate	7	ESISGIPDRFSGSGGTDFTLTISRVESEDFADYVCQINSWPT-----TFGQGTKLEI-KRT

FIG. 21B

Low Risk Light Chain Vs. Kabat Vk3 Consensus; AA54 changed back to murine:**Protein Seq:**

EIVLTQSPGTLVSPGERVTFSCRASQSIGTSIHWYQKQTGQSPRLLIKYASESISGIPDRFSGSGSDFTLTISRVESEDFADYYCQQINSWPTTFGQGTKLEIKRT

Nucleotide Seq:

GAAATAGTCCTTACCCAATCTCCCGGAACCCCTCTCAGTATCTCCCGGGAACGAGTAACCTTTTCATGTAGAGCATCCCAATCCATCGGCACTTCAATTCACT
GGTATCAGCAGAAAAACAGGTCAATCCCCACGGCTTCTTATAAAATATGCATCAGAAATCAATTTCTGGCATCCCGACAGACAGATTTTCAGGTTTCAGGATCAGGCA
CCGATTTACACACTTACAATATCCAGAGTCGAATCAGAAAGATTTTCAGATTACTATTGTCAACAATAAACAGCTGGCCCACTACATTTCGGACAAGGCACAA
AACTCGAAATTAAACGTACG

Low Risk + Moderate Risk Light Chain Vs. Kabat Vk3 Consensus; AA54, 55, 56 changed back to murine:**Protein Seq:**

EIVLTQSPGTLVSPGERVTFSCRASQSIGTSIHWYQKQTGQAPRLLIKYASESISGIPDRFSGSGSDFTLTISRVESEDFADYYCQQINSWPTTFGQGTKLEIKRT

Nucleotide Seq:

GAAATAGTCCTTACTCAATCCCCCGGTACACTCTCAGTTTCCCCAGGGAACGGCTCACTTTTCTTGCGAGCATCAAAATCAATCGGCACTTCAATTCAAT
GGTATCAACAAAAACAGGACAGGCCCCACGACTTCTTATAAATATGCATCAGAAATCAATTTCTGGCATCCCGACAGACAGATTTTCAGGTTTCAGGATCAGGCA
CCGATTTACACACTTACAATATCCAGAGTCGAATCAGAAAGATTTTCAGATTACTATTGTCAACAATAAACAGCTGGCCCACTACATTTCGGACAAGGCACAA
AACTCGAAATTAAACGTACG

FIG. 22A

Light Chain – Changes based on HK6 2-1-1(A14)

V-Region	No. of Changes	Amino Acids 1-52
Risk		LHLHLMLMLMLHLMLLLHLHLHMLHHHHHHHHHHMLMLLMMHHHHHHH
Mouse		DILLTQSPAILSVSPGERVSFSCRASQSIGTSIH----WYQRTNGSPRLLIKYAS
Human		DVVMTQSPAFLSVTPGEKVITTCQASEGIGNLY----WYQKPDQAPKLLIKYAS
Low Risk	10	DIVLTQSPAFLSVTPGEKVFTFCQASQSIGTSIH----WYQKTDQSPRLLIKYAS
Low+Mod	12	DIVLTQSPAFLSVTPGEKVFTFCQASQSIGTSIH----WYQKTDQAPKLLIKYAS

V-Region	No. of Changes	Amino Acids 53-109
Risk		HLMLHMLMLHLHLHLHLHLHLHLHLHLHHHHHHHHHHHHHHHHHLHLHLHLHL
Mouse		ESISGIPSRPFGSGSGTDFTLINSVESEDIADYYCQINSWPT-----TFGGGTKLEI-KRA
Human		QISGVPSRPFSGSGSGTDFTTISSLEAEDAATYYCQGNKHP-----LTFGGGTKVEI-KRT
Low Risk	5	ESISGIPSRPFGSGSGTDFTLTISSEAEADAADYYCQINSWPT-----TFGGGTKLEI-KRT
Low+Mod	5	ESISGIPSRPFGSGSGTDFTLTISSEAEADAADYYCQINSWPT-----TFGGGTKLEI-KRT

FIG. 22B**Low Risk Light Chain vs. VK6 Subgroup 2-1-(1) A14:****Protein Seq:**

DIVLTQSPAFLSVTPGEKVTFTCQASQSIGTSHWYQQKTDQSPRLLIKYASESISGIPSRFSGSGTDFTLTSSVEAEDAADYYCQQINSWPTTFGGGTKLEIKRT

Nucleotide Seq: Not synthesized**Low Risk + Moderate Risk Light Chain vs. VK6 Subgroup 2-1-(1) A14:**

DIVLTQSPAFLSVTPGEKVTFTCQASQSIGTSHWYQQKTDQAPKLLIKYASESISGIPSRFSGSGTDFTLTSSVEAEDAADYYCQQIN
NSWPTTFGGGTKLEIKRT

Nucleotide Seq:

GACATAGTTCTCACACAAATCACCAGCATTCCTCTCAGTTACACCGGCGAAAAAGTAAACCTTTACCTGTCAAGGCTTCTCAATCTATCGGCACCTTCTATTCACT
GGTATCAACAAAAACCGATCAAGCTCTCAATAAATACGCATCCGAATCCATCTCCGGTATCCCTCCAGATTTTCAGGCTCCGGCTCCGGCA
CAGATTTCAACCCTTACCATTAGCTCAGTTGAAGCCGAAGACGCAGCTGATTACTGTCAACAAATAAACTCATGGCCCACTACTTTTCGGCGGCGGCACTA
AACTCGAAATAAAACGTACG

FIG. 23A

Murine RX-1 Light Chain:

DILLTQSPAILSVSPGERVFSRCRASQSIGTSIHWYQORTNGSPRLLIKYASESISGIPSRFSGSGSGTDFTLINSVESEDIADYYCQQINSWPTTFFGGGTEK
LEIKRA

RX1 KV (1) DILLTQSPAILSVSPGERVFSRCRASQSIGTSIHWYQORTNGSPRLLIKYASESISGIPSRFSGSGSGTDFTLINSVESEDIADYYCQQINSWPTTFFG
Consensus Germline LC
hVK I Consensus (1) DIQMTQSPSSLSASVGDRVTITCRASQSLVXX-XISXXLXWYQQKPGKAPKLLIYYXAS
hVK II Consensus (1) DIVMTQSPPLSLPVTGPGEPAISICRSSQSLHSDGNTYLDWYLOKPGQAPRLIIYXYS
hVK III Consensus (1) EIVLTQSPGTLSLSPGERATLSCRASQS-----VSSSYLAWYQQKPGQAPRLIIYXYS
hVK IV Consensus (1) DIVMTQSPDLSAVSLGERATINCKSQSVLYSSNNKNYLAWYQQKPGQAPRLIIYXYS
hVK V Consensus (1) EIVLTQSPAFMSATPDGKVNISCKASQDIDD-D-----DMNHWYQQKPGQAPRLIIYXYS
hVK VI Consensus (1) EIVLTQSPDLSAVSLGERATINCKSQSVLYSSNNKNYLAWYQQKPGQAPRLIIYXYS

LIGHT CHAIN amino half

RX-1 DILLTQSPAILSVSPGERVFSRCRASQSI--GTSIH-----WYQORTNGSPRLLIKYAS

pos... 10 20 30 40 50

Kabat:

HK1...DIQMTQSPSSLSASVGDRVTITCRASQSLVXX-XISXXLXWYQQKPGKAPKLLIYYXAS
HK2...DIVMTQSPPLSLPVTGPGEPAISICRSSQSLHSDGNTYLDWYLOKPGQAPRLIIYXYS
HK3...EIVLTQSPGTLSLSPGERATLSCRASQS-----VSSSYLAWYQQKPGQAPRLIIYXYS
HK4...DIVMTQSPDLSAVSLGERATINCKSQSVLYSSNNKNYLAWYQQKPGQAPRLIIYXYS

Germline Consensus (with JK4):

hVK1 DIQMTQSPSSLSASVGDRVTITCRASQS-----ISSYLNWYQQKPGKAPKLLIYYAAS
hVK2 DIVMTQSPPLSLPVTGPGEPAISICRSSQSLHSDGNTYLDWYLOKPGQAPRLIIYXYS
hVK3 EIVLTQSPGTLSLSPGERATLSCRASQS-----VSSSYLAWYQQKPGQAPRLIIYXYS
hVK4 DIVMTQSPDLSAVSLGERATINCKSQSVLYSSNNKNYLAWYQQKPGQAPRLIIYXYS
hVK5 EIVLTQSPAFMSATPDGKVNISCKASQDIDD-----DMNHWYQQKPGQAPRLIIYXYS
hVK6 EIVLTQSPDLSAVSLGERATINCKSQSVLYSSNNKNYLAWYQQKPGQAPRLIIYXYS

FIG. 23B

LIGHT CHAIN carboxy half

RX-1 ESISGIPSRFSGSGGTDFTLTINSVESEDIADYYCQINSWPT-----TFGGGTKLEI-KRA

pos... 60 70 80 90 abcdef 100 a

Kabat:

HK1...XLXSGVPSRFSGSGGTDFTLTISLQPEDFATYYCQXXXXPE-----XTFGQGTKVEI-KRT
 HK2...NRXSGVPDRFSGSGGTDFTLKISRVEAEDVGYVYCMQAXQXPR-----XTFGQGTKVEI-KRT
 HK3...SRATGIPDRFSGSGGTDFTLTISRLEPEDFAVYVYCCQYGSSPP-----XTFGQGTKVEI-KRT
 HK4...TRESGVDPDRFSGSGGTDFTLTISLQAEADVAVYVYCCQYYSTP-----XTFGQGTKVEI-KRT

Germline Consensus (with JK4):

hVK1 SLQSGVPSRFSGSGGTDFTLTISLQPEDFATYYCQYSYSTP-----LTFGGGTKVEI-KRT
 hVK2 YRASGVDPDRFSGSGGTDFTLKISRVEAEDVGYVYCMQRIEFP-----LTFGGGTKVEI-KRT
 hVK3 SRATGIPDRFSGSGGTDFTLTISRLEPEDFAVYVYCCQYGSSP-----LTFGGGTKVEI-KRT
 hVK4 TRESGVDPDRFSGSGGTDFTLTISLQAEADVAVYVYCCQYYSTP-----LTFGGGTKVEI-KRT
 hVK5 TLVPGIPPRFSGSGYGTDFTLTINNIESEDAAYFCLQHDNFP-----LTFGGGTKVEI-KRT
 hVK6 QSFSGVPSRFSGSGGTDFTLTINSLEAEDAATYYCHQSSSLP-----LTFGGGTKVEI-KRT

FIG. 24A

Murine RX-1 Heavy Chain:

DVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGYISYSGSTSYNPSLSKRSISITRDTSKNQFFLQLSNVTTEDTATYYC
ASFDYAHAMDYWGQGTSTVTVSS

RX1 VH (1) D VQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGYISYSGSTSYNPSLSKRSISITRDTSKNQFFLQLSNVTTEDTATYYCASFY
Consensus Germline
hVH I Consensus (1) QVQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIX--YMHVVRQAPQGLEWMGXIXPY--XXGXT
hVH II Consensus (1) QITLKESGPTLVKPTQTTLTCTFSGFSLSTSGVGVGWIRQPPGKALEWLALIIY--WNDDK
hVH III Consensus (1) E VQLVESGGGLVQPGGSLRLSCAASGFTSS--YMMSVVRQAPGKLEWVANIK--QDGSEK
hVH IV Consensus (1) QVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGYISYSGSTSYNPSLSKRSISITRDTSKNQFFLQLSNVTTEDTATYYC
hVH V Consensus (1) E VQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIX--YMHVVRQAPQGLEWMGXIXPY--XXGXT
hVH VI Consensus (1) QVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGYISYSGSTSYNPSLSKRSISITRDTSKNQFFLQLSNVTTEDTATYYC
hVH VII Consensus (1) QVQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIX--YMHVVRQAPQGLEWMGXIXPY--XXGXT

HEAVY CHAIN amino half

DVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGYIS--YSGST

pos ... 10 20 30 40 50 abc

Kabat:

HH1 ...XVQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIX--WVRQAPQGLEWMGXIXPY--XXGXT
HH2 ...QVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGXIXPY--XXGXT
HH3 ...EVQLVESGGGLVQPGGSLRLSCAASGFTSSYIMX--WVRQAPGKLEWVXXIXXXKXXGXXT

Germline Consensus (with JH4):

hVHI QVQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIMH--WVRQAPQGLEWMGXINP--NSGGT
hVHII QITLKESGPTLVKPTQTTLTCTFSGFSLSTSGVGVGWIRQPPGKALEWLALIIY--WNDDK
hVHIII EVQLVESGGGLVQPGGSLRLSCAASGFTSSYIMH--WVRQAPGKLEWVANIK--QDGSEK
hVHIV QVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGXIXPY--XXGXT
hVHV V EVQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIMH--WVRQAPGKLEWVXXIXXXKXXGXXT
hVHVI QVQLQESGPGGLVKPSQSLTCTVTDYISITSDYAWNWIROFPGNKLEWMGXIXPY--XXGXT
hVHVII QVQLVQSGAEVKKPKGASVVKVSCKASGYTFXSYIMH--WVRQAPGKLEWVXXIXXXKXXGXXT

FIG. 24B

HEAVY CHAIN carboxy half

SYNPSLKSRISTRDTSKNQFFLQLNSVTTEDTATYYCASFDYAHAM-----DYWGQGTSTVTVSS
pos ... 60 70 80 90 100 110
abcde fghijk

Kabat:

HH1 ...NYAQKFQGRVTITXDXTSTAYMELSSRLSRXDTAVYYCARXXXXXXXXXXDXFXFXWGQGTLLVTVSS
HH2 ...XYNPSLKSRLTISVDTSKNQFSLXLXSVTAADTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS
HH3 ...YYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS

Germline Consensus (with JH4):

hVHI NYAQKFQGRVTMTRDTSISTAYMELSSRLSRDSDTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS
hVHII RYSPSLKSRLTITKDTSKNQVLTMTNMDPVDATYYCAHXXXXXXXXXXFXFXWGQGTLLVTVSS
hVHIIL YYVDSVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS
hVHIV NYNPSLKSRLTISVDKSKNQFSLKLSVTAADTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS
hVHV RYSPSFQGVTTISADKSI STAYLQWSSLKASDTAMYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS
hVHVI DYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS
hVHVII TYAQGTGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARXXXXXXXXXXFXFXWGQGTLLVTVSS

Figure 24C:**Kabat numbering of 5H4:****5H4 heavy chain protein sequence:**

1-30: EIQLQQSGPE LVKTGTSVKI SCKASGYSFT
31-35: GYFMH
36-49: WVKQSHGKSLEWIG
50-65: YIS C (52A) YNGDTNY NQNFKG
66-94: KATF TVDTSSSTAY MQF N (82A) S(82B) L(82C) TSED SAVYYCAR
95-102: EGGNYPAY
103-437: WGQG TLVTVSAAKT TPPSVYPLAP GSAAQTNSMV
TLGCLVKGYFPEPVTVTWNS GSLSSGVHTF PAVLQSDLYT LSSSVTVPS TWPSETVTCN
VAHPASSTKV DKKIVPRDCG CKPCICTVPE VSSVFIFPPK PKDVLITITLT PKVTCVVVDI
SKDDPEVQFS WFDVDDVEVHT AQTQPREEQF NSTFRSVSEL PIMHQDWLNG KEFKCRVNSA
APPAPIEKTI SKTKGRPKAP QVYTIPPPKE QMAKDKVSLT CMITDFFPED ITVEWQWNGQ
PAENYKNTQP IMDTDGSYFV YSKLNVQKSN WEAGNTFTCS VLHEGLHNHH TEKSLSHSPG K

5H4 light chain protein sequence:

1-23: DIVMTQSHKF MSTSVGDRVT ITC
24-34: KASQNVG TAVT
35-49: WYQQKPGQSPKLLIY
50-56: WTSTRHA
57-88: GVPD RFTGSGSGTD FTLTISDVQS EDLADYFC
89-97: QQYSSYPLT
98-214: FGAGTKLELKRAD APTVSIFFP SSEQLTSGGA SVVCFLNNFY PKDINVKWKI
DGSERQNGVL NSWTDQDSK STYSMSSTLT LTKDEYERHN SYTCEATHKT
STSPIVKSFN RNEC

Figure 24D:

Kabat numbering of MC1

MC-1 heavy chain protein sequence:

1-30: EVKLVESGGG LVQPGGSLKL SCATSGFTFS
31-35: DYYMY
36-49: WVRQTPEKRLEWVA
50-65: YIS N (52A) GGGSTYY PDTVKG
66-94: RFTI SRDNAKNTLY LQM S (82A) R (82B) L (82C) KSED TAMYYCAR
95-102: QGSYGYPFAY
103-449: WG QGTLVTVSAA KTTAPSVYPL APVCGDTTGS SVTLGCLVKG YFPEPVTLTW
NSGSLSSGVH TFPVAVLQSDL YTLSSSVTVT SSTWPSQSIT CNVAHPASST KVDKKIEPRG
PTIKPCPPCK CPAPNLLGGP SVFIFPPKIK DVLMSLSPI VTCVVVDVSE DDPDVQISWF
VNNVEVHTAQ TQTHREDYNS TLRVVSALPI QHQDWMSGKE FKCKVNNKDL PAPIERTISK
PKGSVRAPQV YVLPPPEEEM TKKQVTLTCM VTDFMPEDIY VEWTTNNGKTE LNYKNTEPVL
DSDGSYFMYS KLRVEKKWV ERNSYSCSVV HEGLHNHHTT KSFSRTPGK

MC-1 light chain protein sequence:

1-23: AIQMTQTTSS LSASLGDRVT ISC
24-34: SASQGIS NYLN
35-49: WYQQKP DGTVKLLIY
50-56: YTSSLHS
57-88: GVPS RFSGSGSGTD YSLTISNLEP EDIATYYC
89-97: QQ YSKLPWT
98-214: FGGGTKLEIKRAD AAPTVSIFPP SSEQLTSGGA SVVCFLNNFY PKDINVKWKI
DGSERQNGVL NSWTDQDSKD STYSMSSTLT LTKDEYERHN SYTCEATHKT STSPIVKSFN
RNEC

Figure 24E**Kabat numbering of MC3****MC-3 heavy chain protein sequence:**

1-30: DVQLQESGPG LVKPSQSLSL TCTVTGYSIT
31-35: SDYAW N (35A)
36-49: WIRQ FPGNKLEWMG
50-65: YISYSGSTSY NPSLKS
66-94: RISIT RDTSKNQFFL QL N (82A) S (82B) V (82C) TTEDT ATYYCAR
95-102: LETWLFDY

103-522: WGQG TTLTVSSAKT TPFSVYPLAP GCGDTTGSSV TLGCLVKGYF PESVTVTWNS
GSLSSSVHTF PALLQSGLYT MSSSVTVPS TWPSTVTCS VAHPASSTTV
DKKLEPSGPI STINPCPPCK ECHKCPAPNL EGGPSVFIFP PNIKDVLMS
LTPKVTCVVV DVSEDDPDVQ ISWVFNNEV HTAQQTQTHRE DYNSTIRVVS
TLPIQHGDWM SGKEFKCKVN NKDLPSPIER TISKIKGLVR APQVYILPPP
AEQLSRKDVS LTCLVVGFPN GDISVEWTSN GHTEENYKDT APVLDSGDSY
FIYSKLNMT SKWEKTSFS CNVRHEGLKN YYLKKTISRS PGLDLDDICA
EAKDGELDGL WTTITIFISL FLLSVCYSAS VTLFKVKWIF SSVVELKQKI
SPDYRNMIGQ GA

MC-3 light chain protein sequence:

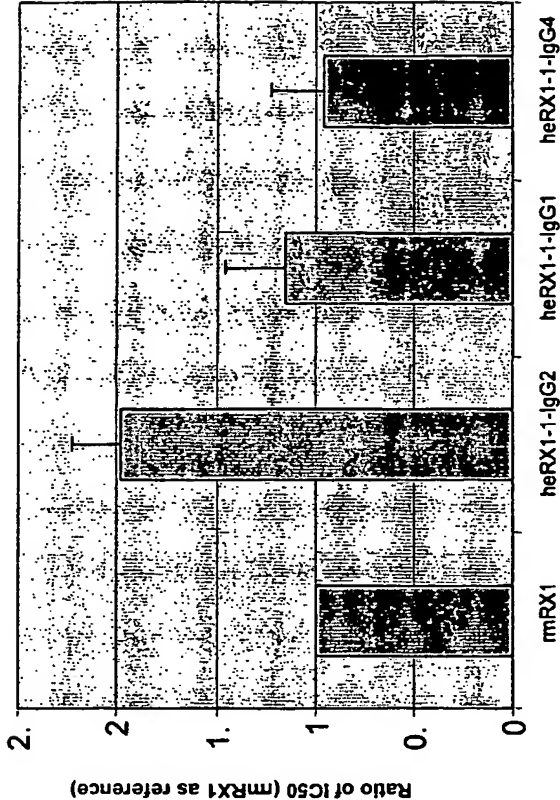
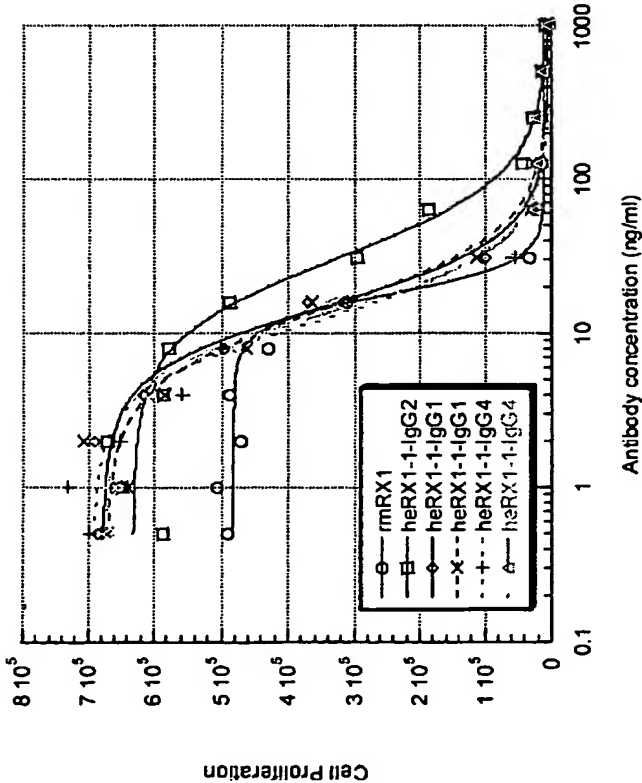
1-23: DILLTQSPAI LSVSPGERVS FSC
24-34: RASQSIG TSIH
35-49: WYQRT NGSPRLLIK
50-56: YASESIS
57-88: GIPS RFGSGSGTD FTLSINSVES EDIADYYC
89-97: QQ SNSWPTT
98-214: FGG GTKLEIKWAD AAPTVSIFPP SSEQLTSGGA SVVCFLNNFY PKDINVWKI
DGSERQNGVL NSWTDQDSK STYSMSSTLT LTKDEYERHN SYTCEATHKT
STSPIVKSFN RNEC

Fig. 25

Measurement of Neutralizing Activity of heRX1 With Different IgG Subclass Constant Regions

Neutralizing activity of heRX1-1 series

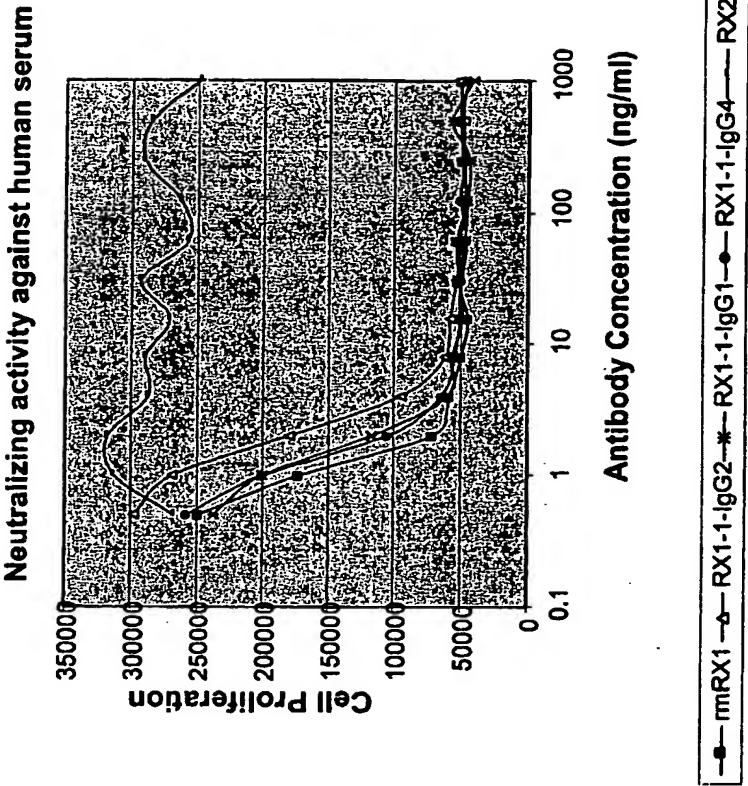
Neutralizing activity of heRX1-1 with human Constant



Against recombinant human MCSF

Fig. 26

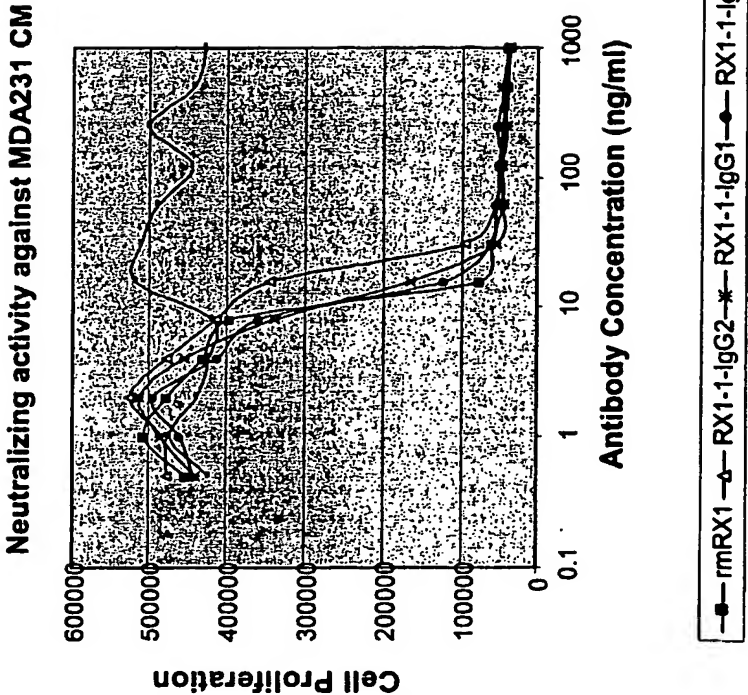
Activity of heRX1-1 With Different IgG Subclasses Against Other Forms of MCSF



Similar results observed against Cyno MCSF in serum and recombinant Cyno MCSF

Fig. 27

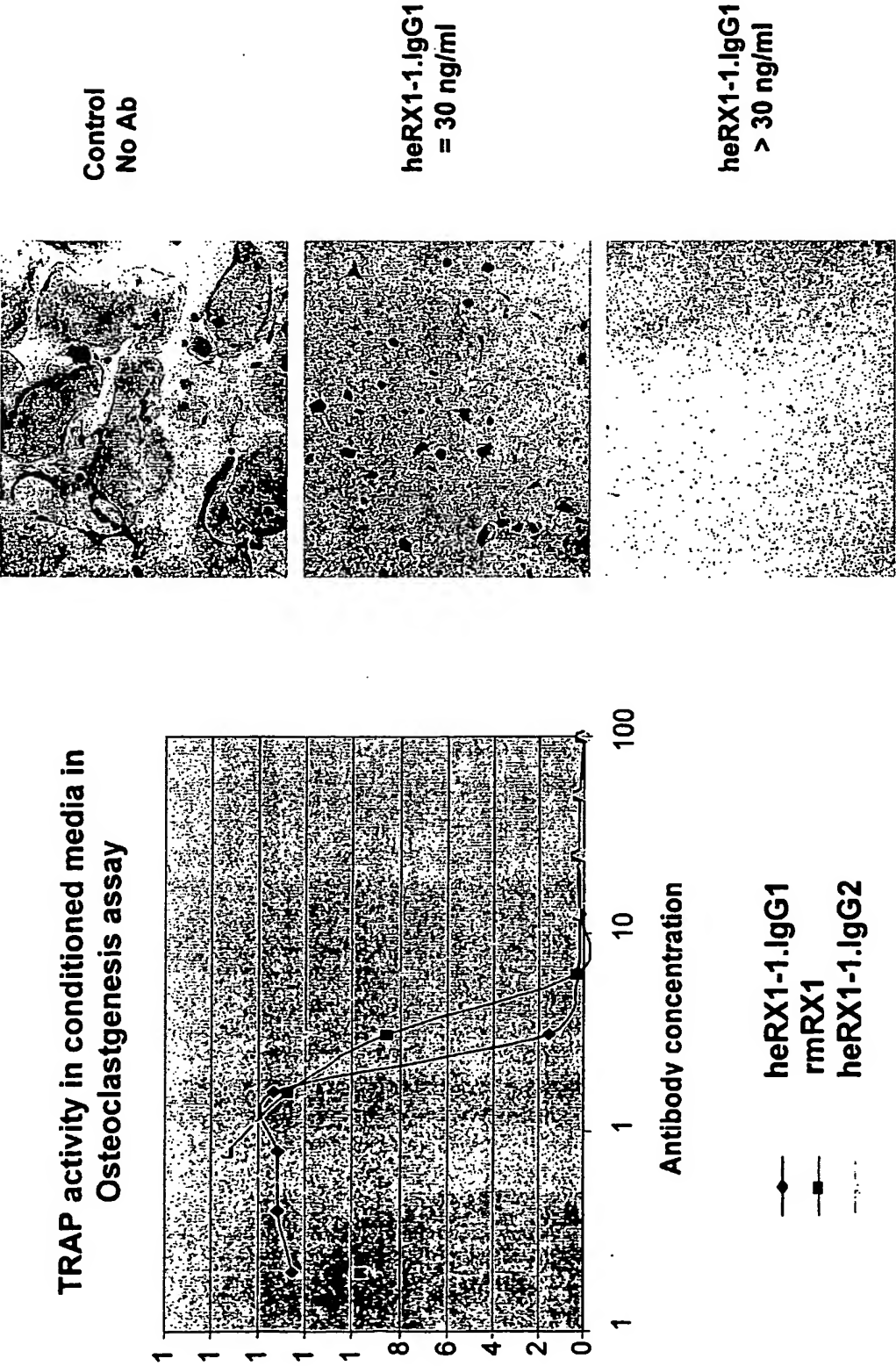
Activity of heRX1-1 With Different IgG Subclasses Against Other Forms of MCSF



Similar results observed against Cyno MCSF in serum and recombinant Cyno MCSF

Fig. 28

Osteoclastogenesis Assay of heRX1-1 With Different IgG Subclasses



Amino Acids

MGWSCILFLVATATGVHS

DVQLQESGPGLVKPSQTLSTCTVTDYSITSDYAWNWIRQFPGKKLEWMGYISYSGSTSYPNPSLKSRTISRDTSKNQFSL
QLNSVTAADTATYYCASFDYAHAMDYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTY
ICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE
MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH
YTQKSLSLSPGK•

Nucleotides

ATGGGATGGAGTTGCATTATACTTTTCTCGTTGCCACCGCCACTGGAGTTCCTGACGTACAACCTTCAAGAATC
TGGCCCAGGTCTCGTCAAACCTTCTCAAACCTCTCTCACTCACCTGCACTGTTACTGACTACTCTATTACATCCGACTA
CGCTTGGAACCTGGATCCGACAATTTCTGGTAAAAAACTCGAATGGATGGGTTATATTTCTTACTCTGGCTCCACCT
CCTACAATCCTTCTCTGAAATCACGCATCACAAATTTCCCGCGATACCTCTAAAAATCAATTTTCACTCCAACCTCAATT
CTGTTACCGCCGCCGATACTGCCACCTACTACTGTGCCTCTTTTGACTACGCTCACGCCATGGATTATTGGGGACAG
GGTACTACCGTTACCGTAAGCTCAGCCAGCACAAAGGGCCCATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCA
CCTCTGGGGGACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAATC
AGGCGCCCTGACCAGCGGCGTGACACCTTCCCGGCTGTCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGG
TGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGT
GGACAAAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGTCCACCGTGCCCAGCACCTGAACTCCTGGGG
GGACCGTCAGTCTTCTCTTCCCCCAAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTACATGCGT
GGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGC
CAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGA
CTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCC
AAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAG
GTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGG
AGAACAACCTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTATAGCAAGCTCACCGTGGAC
AAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGTCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGA
AGAGCCTCTCCCTGTCCCCGGGTAAATGA

Amino Acids

MGWSCILFLVATATGVHS

QVQLQESGPGLVKPSQTLSTCTVSDYSITSDYAWNWIQFPKGLEWMGYISYSGSTSYNPSLKSRIITSRDTSKNQFSL
QLNSVTAADTAVYYCASFDYAHAMDYWGQGTTVTVSS

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTY
ICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE
MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH
YTQKSLSLSPGK•

Nucleotides

ATGGGTTGGTCTTGCATCATTCTCTTTCTCGTCGCTACCGCAACTGGTGTACACTCCCAAGTTCAACTTCAAGAATCA
GGCCCCGGACTCGTTAAACCCTCTCAAACCTCTCTCTTACTTGCACTGTATCCGATTACTCTATTACTTCAGACTAC
GCTTGGAAGTGGATCAGACAATTTCCCGGAAAAGGACTCGAATGGATGGGATATATCTCTTACTCTGGCTCAACCT
CTTACAACCCCTCTCTCAAATCTCGAATAACAATCTCACGCGATACTTCTAAAAATCAATTCTCACTTCAACTTAAC
TCCGTTACTGCCGCCGACACTGCCGTTTACTACTGTGCTTCCTTCGATTACGCCCACGCTATGGATTATTGGGGACA
AGGAACTACCGTCACTGTCAGCTCAGCCAGCACAAAGGGCCCATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGC
ACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAAGT
CAGGCGCCCTGACCAGCGGCGTGACACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTG
GTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGG
TGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGTCCACCGTGCCAGCACCTGAACTCCTGGG
GGGACCGTCAGTCTTCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCG
TGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG
CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGG
ACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTC
CAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCA
GGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCG
GAGAACAACTACAAGACCACGCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTATAGCAAGCTCACCGTGG
ACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCA
GAAGAGCCTCTCCCTGTCCCCGGGTAAATGA

Fig. 30

HeRX-1 Low Risk Heavy Chain Gamma-4

Amino Acids

MGWSCILPEVATATGVHSDVQLQESGPGLVKPSQTLSTCTVTDYSITSDYAWNWIQFPGKKLEWMGYISYSGSTSYN
PSLKSRITISRDTSKNQFSLQLNSVTAADTATYYCASFDYAHAMDYWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTA
ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKY
GPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTKSKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK

Nucleotides

cDNA

ATGGGATGGAGTTGCATTATACTTTTCTCGTTGCCACCGCCACTGGAGTTCACCTCTGACGTACAACCTTCAAGAATC
TGGCCCAGGTCTCGTCAAACCTTCTCAAACCTCTCTCACTCACCTGCACTGTTACTGACTACTCTATTACATCCGACTA
CGCTTGAACTGGATCCGACAATTTCTGGTAAAAAACTCGAATGGATGGGTTATATTTCTTACTCTGGCTCCACCT
CCTACAATCCTTCTCTGAAATCACGCATCACAATTTCCCGCGATACCTCTAAAAATCAATTTTCACTCCAACCTCAATT
CTGTTACCGCCGCGGATACTGCCACCTACTACTGTGCCTCTTTGACTACGCTCACGCCATGGATTATTGGGGACAG
GGTACTACCGTTACCGTAAGCTCAGCCAGCACAAGGGGCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCA
CCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCT
AGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGG
TGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAACACCAAGGT
GGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCCCATCATGCCAGCACCTGAGTTCCTGGGGGGACCATCA
GTCTTCTGTGTTCCCCCAAACCCAAAGGACACTCTCATGATCTCCCGGACCCCTGAGGTACGTGCGTGGTGGTGA
CGTGAGCCAGGAAGACCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAAGACAAA
GCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCTCACCCTCCTGCACCAGGACTGGCTGAAC
GGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCCCGTCTCCATCGAGAAAACCATCTCCAAAGCCAAA
GGGACGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTG
ACCTGCCTGGTCAAAGGCTTCTACCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAAC
TACAAGACCACGCTCCCGTGTCTGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTAACCGTGGACAAGAGCA
GGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACACAGAAGAGCCT
CTCCCTGTCTCTGGGTAAATGA

Genomic

ATGGGATGGAGTTGCATTATACTTTTCTCGTTGCCACCGCCACTGGAGTTCACCTCTGACGTACAACCTTCAAGAATC
TGGCCCAGGTCTCGTCAAACCTTCTCAAACCTCTCTCACTCACCTGCACTGTTACTGACTACTCTATTACATCCGACTA
CGCTTGAACTGGATCCGACAATTTCTGGTAAAAAACTCGAATGGATGGGTTATATTTCTTACTCTGGCTCCACCT
CCTACAATCCTTCTCTGAAATCACGCATCACAATTTCCCGCGATACCTCTAAAAATCAATTTTCACTCCAACCTCAATT
CTGTTACCGCCGCGGATACTGCCACCTACTACTGTGCCTCTTTGACTACGCTCACGCCATGGATTATTGGGGACAG
GGTACTACCGTTACCGTAAGCTCAGCCAGCACAAGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCA
CCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTC
AGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGG
TGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAACACCAAGGT
GGACAAGAGAGTTGGTGAAGAGGCCAGCACAGGGAGGGAGGGTGTCTGCTGGAAGCCAGGCTCAGCCCTCCTGCCT
GGACGCACCCCGGCTGTGCAGCCCCAGCCAGGGCAGCAAGGCATGCCCCATCTGTCTCCTCACCCGGAGGCCTCT
GACCACCCCACTCATGCTCAGGGAGAGGGTCTTCTGGATTTTTCACCAGGCTCCGGGCAGCCACAGGCTGGATGC
CCCTACCCAGGCCCTGCGCATACAGGGGCAGGTGCTGCGCTCAGACCTGCCAAGAGCCATATCCGGGAGGACCT
GCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCACTCCCTCAGCTCAGACCTTCTCTCCTCCCAGATCTG
AGTAAGTCCCAATCTTCTCTCTGCAGAGTCCAAATATGGTCCCCCATGCCCATCATGCCAGGTAAGCCAACCCAGG
CCTCGCCCTCCAGCTCAAGGCGGGACAGGTGCCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTG
ACGCATCCACCTCCATCTCTTCTCAGCACCTGAGTTCCTGGGGGGACCATCAGTCTTCTGTTCCCCCAAACCC
AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTACGTGCGTGGTGGTGGACGTGAGCCAGGAAGACCCCGAGG
TCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTTCAACA
GCACGTACCGTGTGGTCAGCGTCTCACCCTCCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGT
CTCCAACAAAGGCCTCCCGTCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCACGGGTGCGAGG
GCCACATGGACAGAGGTGAGCTCGGCCACCCCTCTGCCCTGGGAGTGACCGCTGTGCCAACCTCTGTCCCTACAGG
GCAGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGAC
CTGCCTGGTCAAAGGCTTCTACCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGGAACAATA
CAAGACCACGCTCCCGTGTCTGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTAACCGTGGACAAGAGCAGG
TGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACACAGAAGAGCCTCT
CCCTGTCTCTGGGTAAATGA